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## THE PROTEIN PROBLEM OF CHINA<sup>1</sup>

By Dr. WILLIAM H. ADOLPH

CORNELL UNIVERSITY; UNTIL RECENTLY PROFESSOR OF BIOCHEMISTRY, YENCHING UNIVERSITY, PEKING

### PROTEIN INTAKE

THE protein problem of China implicates the nutrition problem of China as a whole. Our experience in the Far East leads us to believe that in normal times the question of sufficient calories usually takes care of itself. That is to say, in a closed area or in a large agricultural country undisturbed by much industry, when the population pressure is in equilibrium with the food supply, it would appear that people live or die, depending upon whether the supply of calories is sufficient or not. This is one reason incidentally why the problem of nutrition in China is such a fascinating one for the food economist; the equilibrium is such a simple straightforward equilibrium with very few side reactions. But aside from calories the question of protein is probably the first qualitative factor

of importance. Our first set of data published about twenty years ago indicates a protein intake of approximately 80 grams per capita per day,<sup>2</sup> which figure subsequent studies have confirmed as an average statement of the protein intake.

### THE RURAL DIET IS VEGETARIAN

A further accounting shows that about 95 per cent. of this average protein intake is derived from vegetable sources, while 5 per cent. is animal protein. One should hasten to explain that these figures are for the Chinese rural diet, which accounts for some 85 to 90 per cent. of the total population of the country. Please keep in mind that those who live in the more sophisticated centers, including those citizens of China whom we meet on the college campuses of this country, are accustomed to a dietary which approximates in character and variety that of the Occident.

<sup>1</sup> Paper presented at a Symposium on the Biological Value of Proteins, at the Cleveland Meeting of the American Chemical Society, April 6, 1944.

<sup>2</sup> W. H. Adolph, *Jour. Home Econ.*, 17: 1, 1925.



They represent, however, but a small percentage of the total population. Taking the country as a whole, therefore, with its 400,000,000 of population, and keeping in mind particularly the large agricultural areas of the interior we have here a very close approximation to a real vegetarian diet on a large scale!

Now, if the average protein intake is reckoned at 80 grams per day and the average body weight of the Chinese at 55 kilograms, it would seem that the standard protein requirement of one gram per kilo has been met. However, when the coefficient of digestibility of the protein, as it is actually encountered in the diet, is considered, it is evident that the real intake is much lower. Moreover, when the biological value of the protein is considered, it is readily understood that the average Chinese diet may be really deficient in protein.

#### COEFFICIENT OF DIGESTIBILITY

The coefficient of digestibility for animal protein is usually taken as about 92. The figures which we have determined for protein in the typical Oriental vegetarian diet range from 55 to 80, with an average of about 65. In dietary studies involving protein intake on vegetarian diets, this low digestibility is not usually taken into account. There is the possibility of a general roughage effect due to the great bulk of the food. It has not been possible to distinguish clearly between what is strictly a roughage effect, *i.e.*, a reduced digestibility due mainly to the large bulk of the diet, and that due to an intrinsically low digestibility of the protein material. There is no question whatever that the vegetarian diet may be extremely bulky, but our experience, primarily with laboratory animals, leads us to suspect that bulk itself does not greatly interfere with digestibility. In metabolism experiments using diets consisting of sweet potatoes and cereals, we have found fecal nitrogen as high as 3 or 4 grams per day. Some of this may represent metabolic nitrogen, of course, but in any event it represents an equivalent somewhere in the balance sheet of say 20 to 25 grams of protein daily.

One of the problems in the Far East involving the coefficient of digestibility is in the use of polished rice. The digestibility of rice is increased with the degree of polishing. But it becomes necessary to balance carefully the advantages which may result from increased polishing against the accompanying losses in vitamins. And this calculation involves the welfare of the rice-eating fraction of the population, say 300,000,000 people. It is clear that the factor of digestibility must not be overlooked.

#### BIOLOGICAL VALUE

The biological values of most of the cereal and vegetable proteins used in the Orient have been determined by standard methods. Milk and egg proteins

which do not figure largely in the Oriental dietaries have high biological values, say 88 to 94, when determined by Mitchell's method, while the proteins that do figure conspicuously in the Oriental dietaries show values which lie usually between 50 and 75. Proteins which do not interest the Occident have been of considerable interest to us in China, the protein of celery cabbage and the protein of sweet potato, for example, which have biological values of 76 and 72 respectively,<sup>3</sup> and these two together in many rural dietaries may comprise a very considerable fraction of the protein intake.

#### SUPPLEMENTARY VALUE: MIXED CEREAL PROTEINS

It is of interest to discover that in the rural, cereal-consuming areas of north China, in spite of the tendency toward simple and rather monotonous diets, the cereals consumed, whether as cooked cereal or in the form of a bread, are usually not single cereals, but are mixed cereals. The mixtures, moreover, follow definite proportions, which differ in different areas, but proportions which have been fixed apparently over many centuries. We have determined the biological values of these cereal mixtures and have invariably found the biological values much higher than those of single cereals.<sup>4</sup> It would appear that in each area, within the limits of the agricultural conditions prevailing in that area, a formula has been worked out which provides a protein mixture of high biological value, if not of maximum value. This may be another case of blind experimentation, examples of which are wide-spread throughout Asia. The rural peoples are generally prepared with a ready response when questioned regarding the relative nutritive value of the food items used in that area. They may state that this food "stays with you" or that food "furnishes muscular vigor." One of our pastimes has been that of checking up these rural opinions and finding that they often correspond closely to estimates of nutritive value made in the laboratory.

Now on the practical side we are very much interested in another type of supplementary protein. Wan and Lee<sup>5</sup> found that the best vegetarian diet that they could devise for laboratory animals had a biological value of 74. By the simple device of adding a small per cent. of dried beef to the diet the biological value was increased to over 80. The implications involved in this are self-evident.

#### CELERY CABBAGE PROTEIN

Of the vegetable proteins, the nutritionists in China are suggesting the larger use of the leaf vegetable

<sup>3</sup> H. C. Kao, W. H. Adolph and H. C. Liu, *Chinese Jour. Physiol.*, 9: 141, 1935.

<sup>4</sup> W. H. Adolph and F. W. Cheng, *Chinese Jour. Physiol.*, 9: 245, 1935.

<sup>5</sup> S. Wan and W. Y. Lee, *Chinese Jour. Physiol.*, 5: 157, 1931.

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proteins, with particular attention directed toward the well-known celery cabbage. It has been proposed that leaf vegetables be used to replace some of the cereal which now constitutes 88 per cent. of the rural dietary. Animal experiments<sup>6</sup> followed by experiments with human subjects have indicated that this is possible. And of course this has the advantage not only of increasing the amount of good protein in the diet but also that of calcium and other important accessories. When added to a basal cereal diet it made little difference whether the celery cabbage was fed in fresh or in dried form. In these experiments maximum growth was obtained when the celery cabbage constituted on a dry basis 20 per cent. of the mixture. At the same time the celery cabbage-cereal mixed protein showed a slightly higher biological value. A large-scale dairy industry would be economically impossible in China at present, but it is believed that the farm economy could effect such an adjustment as this, involving slightly more green vegetable and slightly less cereal with satisfactory results and without seriously disturbing the economic *status quo*.

#### ANIMAL PROTEIN VS. VEGETABLE PROTEIN

In the laboratory of the Peking Union Medical College, Dr. Hsien Wu<sup>7</sup> over a period of 10 or 15 years has conducted experiments on the subject of vegetarian vs. omnivorous diet, using laboratory rats. He has shown in the first place that an omnivorous diet, i.e., one consisting of both animal and vegetable food materials, is superior to the best vegetarian diet that they have been able to devise. A very large number of simple vegetarian diets were tried, and vegetarian combinations in every shape and form. The superiority of the omnivorous diet has been measured in terms of growth, of reproduction, performance of work. They show that the superiority of the omnivorous diet is largely due to the superiority of the animal protein over the vegetable protein, although of course the vegetarian diet also tends to be deficient in other factors as well.

#### PROTEIN IN THE WAR ECONOMY

A war economy inevitably leads to the use of more vegetable food, with a corresponding decrease in the amount of animal products consumed. This urge is accompanied by the statement that more people can be fed by such an arrangement. This is probably a step in the right direction as a temporary war measure, and with enriched cereals and other enriched vegetable products much large-scale relief may be possible, but our observations in the Far East lead us to

interpose a note of caution. Such an arrangement must be carefully controlled and carried out with a thorough understanding of the implications involved in the vegetarian diet. Do we know, for example, how far the change from the omnivorous diet to the vegetarian can be carried with impunity? Many of our blessings in health and vigor are, nutritionally speaking, related to animal protein. Our experiences in the internment camps emphasized again that attempts to change too radically the dietary pattern of a group of Occidentals was usually not attended with success. America desires to share and to be of assistance to the other peoples of the world, and at the same time desires to maintain the efficiency of the American worker in the war effort. The question may be raised as to how far we should undertake to change a dietary pattern which so far has served us well in the war effort.

#### NUTRITIONAL EDEMA

It is difficult to point specifically to certain factors in the physical make-up of the peoples of rural China as due to protein deficiencies. Cases of nutritional edema, however, are not unusual. When such cases are fed a diet containing a liberal amount of animal protein, the serum protein is usually promptly restored to the normal level. Ling<sup>8</sup> reports a group of 24 famine subjects so treated and the edema was cured in about two months. In general, the item of poor protein is only one of the factors that enters into the clinical picture in nutritional edema, but it is probably the important one.

#### RECLAMATION OF NITROGEN

Now there is still another angle to the protein problem—the reclamation of nitrogen; and this is a phase to which less attention is given in America. Rural China for centuries has returned to the soil large amounts of the protein wastage from the human metabolic process. In the case of the solid portion of night soil, practically all is collected, but the process of drying, composting or preparing for actual use on the farm is inefficient and not more than 50 per cent. of the nitrogen gets back into the soil.<sup>9</sup> In the case of the liquid portion of night soil somewhat less of the nitrogen than this, about 10 per cent. in north China, 35 per cent. in south China is actually returned to the soil. The studies in composting and use of night soil are among the most important scientific investigations now in progress in China. These studies neglect the esthetics of sewage disposal, but they do represent an attempt to increase the efficiency of the nitrogen conservation process. For rural China we

<sup>6</sup> P. C. Hsu and W. H. Adolph, *Chinese Jour. Physiol.*, 15, 275, 1940.

<sup>7</sup> S. Wan and H. Wu, *Chinese Jour. Physiol.*, 9: 119, 1935.

<sup>8</sup> S. M. Ling, *Chinese Jour. Physiol.*, 5: 1, 1931.

<sup>9</sup> S. D. Wilson and Y. Wang, *Peking Nat. Hist. Bul.*, 13: 269, 1939.



have been using the figure 450 grams as the amount of nitrogen excreted per capita per year. This is an important figure in all calculations. We are omitting mention of one type of nitrogen reclamation cycle in which the soil and agricultural crops are by-passed and excreted nitrogen is used directly for conversion into animal tissues without being converted first into agricultural product!

#### FOOD RELIEF AND REHABILITATION

One of the questions of immediate importance is the problem of food relief. The war in China, which has been under way now for seven years, has badly disturbed the delicately balanced factors of food supply and demand. Not only have 10 million people or more migrated from occupied China into free China, but the army of several more million tends to be fed from the area in which it is stationed. The army itself continues to suffer from a deficient ration. The need as far as it is a need for calories can be met by simply sending in more cereals and organizing transport which will bring these additional calories to the point where they are to be used. But for a long-term relief program something more adequate must be done and there is a growing conviction that it will be desirable to concentrate on proteins. This is not an easy problem. It is only partly economic. A concerted research program is necessary. We will need to know more about some of the less common foods. China has made some use of the soybean, but only to a limited extent. Why?

From one angle a beginning has been made by the agronomists. By crop selection a millet has been pro-

duced which contains over 14 per cent. of protein instead of the usual 9 per cent.; this would represent a possible out-and-out increase of 50 per cent. in the gross protein production. If the need is for a better quality of protein, is the only answer to be found in a meat industry or in a dairy industry? The war and the present cooperative undertakings in China offer an unusual opportunity for a first step in solving these problems. Nutritionists in the Far East have for too long a time concerned themselves merely with the problem of *enough* food. It is appropriate that they now approach the problem of the *right kind* of food.

#### SUMMARY

(1) The protein intake of China is approximately 80 grams per capita per day, 5 per cent. of which is animal protein. (2) The lower digestibility of the protein in vegetarian diets causes the effective protein intake to be much less than is indicated by this figure. (3) Attempts in the laboratory to devise an adequate diet using foods from vegetarian sources only have not met with marked success. (4) The use of mixed cereals in the diet has provided protein of higher biological value; this habit may reflect the attempt on the part of the rural peoples to work out a more effective protein intake. (5) It is suggested that in China some of the cereal protein in the dietary intake be replaced by more leaf vegetable protein. (6) The question is raised as to how far it is feasible in the war economy to replace animal protein by vegetable protein. (7) In long-term plans for food relief in the Far East it is urged that an emphasis be placed on the protein factor.

## OBITUARY

### ARCHIE SCOTT WOODS

THE untimely death of Archie Scott Woods in an automobile accident near San Diego, Calif., on April 20, 1944, is mourned by men of medicine and by the institutions which they serve. Through his association with the John and Mary R. Markle Foundation he was well known to them and had become not only a friend but a sympathetic and eager helper in their efforts to advance medicine in this country. It was in connection with problems in tropical medicine in the Armed Forces in which lately he had become greatly interested that he had journeyed to the West Coast and there met his death. He should be numbered among the casualties of war.

Archie Woods' career was an unpredictable achievement, its starting point a fortunate circumstance. Born in London, Ontario, Canada, in 1895, and spending his early life in eastern Pennsylvania, he had

not, through his parents or family connections, any association with medicine. He graduated from Lafayette College in 1916 with a degree in mechanical engineering and worked for a time for Wood, Dodson and Company, coal operators in Bethlehem, Pa. He later was with E. B. Smith and Company, investment bankers in Philadelphia. In 1925 he went to New York City to be secretary to John Markle, anthracite coal operator and philanthropist. With the formation of the John and Mary R. Markle Foundation in 1927, Archie Woods became its vice-president, treasurer and director. The decision having been reached to devote the funds of the foundation largely to research in medicine, he was entrusted by his board of directors with the responsibility wisely to distribute them.

Thrust into a field of activity of which previously he completely lacked both knowledge and experience, he became an ardent student of medicine and at the

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time of his death few men had a greater appreciation of the trends of research in medicine, a more intimate knowledge of the research in progress throughout the country and a closer association and friendship with the men engaged in it. He made a sincere effort to understand the problems for which grants-in-aid were sought. He adopted the usual practice of seeking advice from medical men regarding the merits of research projects. But in addition he pursued a course of self-education in medicine. His frequent visits to institutions in which research supported by his foundation was in progress, his attendance at medical society meetings, his reading of medical books and journals and particularly, perhaps, his discussions with his medical friends gave him a very considerable knowledge of medicine. He had the ability to assemble and arrange his variously acquired information; and if he could be drawn out, was able to discuss intelligently and with comprehensive knowledge many of the fields of medicine which actively are being advanced to-day.

Archie Woods thoroughly enjoyed his association with medical men. He was eager to assist them in their work; yet was equally concerned that the funds which his board of directors entrusted to him should not be wasted. He had a real skill in judging the merits of research projects submitted to him and the ability to select, for financial support, the promising ones. He was known as honest and fair-minded in his dealings with men and he commanded their respect. In the years of his association with the Markle Foundation he made himself an expert in many matters relating to medicine and an important figure in

the advancement of medical knowledge. Toward the end of his career he, a layman, had become, on occasion, a consultant in medicine; for his advice was sought and his assistance obtained in the organization of some of its teaching and research programs.

GEORGE J. HEUER

NEW YORK HOSPITAL

#### LESTER S. GUSS

LESTER S. GUSS, professor and head of the department of chemistry of South Dakota State College, died following a heart attack on May 17 at the age of forty years. Dr. Guss received the B.S. degree in 1923 and the M.S. degree in 1925 from the University of North Dakota. After teaching in high schools of Minnesota he came to South Dakota State College in 1928 as instructor in chemistry. He continued graduate study in chemistry at the University of Minnesota during 1936-38, receiving the Ph.D. degree at the end of that time. In 1940 he was made head of the chemistry department at South Dakota State College. He held a reserve commission of Captain in the CWS until the spring of 1941, when he resigned in order to better serve his country as a chemist. He worked on the WPB rubber program with Dr. I. M. Kolthoff at the University of Minnesota during 1943, his research covering indicators in anhydrous solvents, acidity in anhydrous solvents and properties of soap solutions. During 1943-44 he was chairman of the Sioux Valley section of the American Chemical Society, and on May 6 was elected president of the South Dakota Academy of Science for the ensuing year.

G. L. BROWN

## SCIENTIFIC EVENTS

### A COLLEGE OF CHEMICAL ENGINEERING AT SÃO PAULO

THE following official announcement of the establishment of a College of Chemical Engineering at São Paulo has been sent to SCIENCE.

Social Action, a Jesuit organization in Brazil, is planning to open in São Paulo a College of Chemical Engineering with a capacity for 1,000 students. Father Saboia de Medeiros, president of Social Action in Brazil, has retained certain officials of the University of Detroit as his advisers.

One of the most important problems is the selection of the faculty. To conform with Brazilian laws, members of the faculty must, except for possibly one or two, have been born in Brazil. But to conform with the educational aims of Father Saboia, the curriculum, the faculty and the facilities must represent the best ideas of chemical engineering education in the United States. This means that those selected as faculty members, in addition to having been born in Brazil, should have had considerable teaching

experience in the United States. However, since instructors in the field of chemical engineering will also need to have had considerable industrial experience, this will make up to a large extent for lack of previous teaching activity. All instruction will be conducted in Portuguese—the official language of the country. Members of the faculty will be appointed in all divisions of chemistry, mathematics, physics, metallurgy, mechanical and electrical engineering, mechanics, chemical engineering, economics, and in business organization and management. It is hoped that a student registration for the first freshman class will be made about March 1, 1945. Members of the faculty will be appointed to meet instructional needs as students enter and as they advance through the curriculum. It will be necessary that all members be practical Catholics.

It is hoped that information about the new college will be extensively circulated in the Catholic educational circles and will be brought to the attention of all Brazilians residing in the United States. Any person desiring to teach



in the above-mentioned fields who feels that he can meet the standards outlined is asked to write to Father George J. Shiple, S.J., director of the department of chemistry of the University of Detroit, Detroit 21, Michigan.

#### DEDICATION OF AN EQUIPMENT MUSEUM AT THE MEDICAL FIELD SERVICE SCHOOL

A FIELD equipment museum section has been established in the Medical Department Equipment Laboratory at the Medical Field Service School, Carlisle Barracks, Pennsylvania. At the dedication on May 17, the principal address was given by Major General George F. Lull, the Deputy Surgeon General. While a small museum of historical equipment has been in existence for several years, during the last two years it has been developed into an exhibit room, with new display cases and many valuable reconstructed models. New models and items of experimental equipment are being added from time to time.

In the equipment sample room in the museum are displayed most of the standard items of Medical Department field equipment. This exhibit was established for the purpose of instructing recently commissioned officers of the Medical Department, thousands of whom have completed the courses at the Medical Field Service School. The sample room was established as a section of the Equipment Laboratory in order to make items of field equipment immediately available to the personnel of the laboratory when considering changes in drawings, design or packaging, and also for comparative study in the development of new equipment.

This display is unique in that the contents of packages, kits and chests are spread out in glass-topped cases with the chest or container being shown under the case. Each display is labeled in accordance with title and item number as given in the Medical Department Supply Catalogue. The display features all the various medical, dental and veterinary field chests and kits and their contents, also pack equipment on pack saddles, Air Forces and Chemical Warfare medical equipment, x-ray units, and laboratory and field hospital equipment and supplies. On the walls of the room are framed pictures of the larger mobile units recently developed—surgical truck, mobile laboratories, dental operating truck, optical repair truck, field ambulances and disinfecter. This display will be kept up to date by prompt requisition of new items and the removal of obsolete or discontinued items, those of the latter having historical interest being transferred to the museum section.

Brigadier General Addison D. Davis is the commanding general at the barracks and Colonel Earle D. Quinnell, M.C., is the director of the Medical Department Equipment Laboratory.

#### OFFICERS OF THE AMERICAN INSTITUTE OF ELECTRICAL ENGINEERS

CHARLES A. POWEL, manager, Headquarters Engineering Departments, Westinghouse Electric and Manufacturing Company, East Pittsburgh, Pa., was elected president of the American Institute of Electrical Engineers for the year beginning August 1, 1944, during the summer technical meeting, as announced at the annual meeting of the institute, held in St. Louis, Mo. The other officers elected were:

*Vice-presidents*, R. T. Henry, Buffalo, N. Y.; J. F. Fairman, New York, N. Y.; M. S. Coover, Ames, Iowa; R. W. Warner, Austin, Texas; C. B. Carpenter, Portland, Ore. *Directors*, P. L. Alger, Schenectady, N. Y.; M. J. McHenry, Toronto, Canada; D. A. Quarles, New York, N. Y. *National Treasurer*, W. I. Slichter, New York, N. Y. (re-elected).

These officers, together with the following hold-over officers, will constitute the Board of Directors for the next administrative year, beginning August 1, 1944:

Nevin E. Funk, Philadelphia, Pa. (retiring president); Harold S. Osborne, New York, N. Y. (junior past president); L. A. Bingham, Boulder, Colo.; L. R. Gamble, Spokane, Wash.; J. M. Gaylord, Los Angeles, Calif.; Walter J. Gilson, Toronto, Canada; K. L. Hansen, Milwaukee, Wis.; C. M. Laffoon, East Pittsburgh, Pa.; T. G. LeClair, Chicago, Ill.; F. R. Maxwell, Jr., Pensacola, Fla.; C. W. Mier, Dallas, Tex.; S. H. Mortensen, Milwaukee, Wis.; W. B. Morton, Philadelphia, Pa.; Claire W. Ricker, New Orleans, La.; W. R. Smith, Newark, N. J.; W. E. Wickenden, Cleveland, Ohio.

The annual report of the Board of Directors, presented at the meeting, showed a total membership on April 30 of 21,407. In addition to three national technical meetings and two district technical meetings, 1,493 meetings were held during the year by the local organizations of the institute in the principal cities and educational institutions of the United States, Canada and Mexico.

H. H. HENLINE,  
*National Secretary*

#### THE AMERICAN GEOPHYSICAL UNION

At the meeting of the American Geophysical Union held in Washington, D. C., on June 2, L. H. Adams was elected president, and W. H. Bucher was elected vice-president. Dr. J. A. Fleming continues as general secretary until June 30, 1946.

The officers of the section for the three-year term beginning on July 1 were elected as follows:

*Geodesy*—W. D. Sutcliffe, *President*; P. Kissam, *Vice-president*; J. A. Duerksen continues as secretary. *Seismology*—V. C. Stechschulte, *President*; Frank Neumann, *Vice-president*; A. Blake continues as secretary. *Meteorology*—F. W. Reichelderfer, *President*; H. R.



Byers, *Vice-president*; H. D. Harradon, *Secretary*.

*Terrestrial Magnetism and Electricity*—H. F. Johnston, *President*; Irwin Roman, *Vice-president*; D. G. Knapp, *Secretary*.

*Oceanography*—H. U. Sverdrup, *President*; W. L. Schmitt, *Vice-president*; L. P. Disney, *Secretary*.

*Volcanology*—R. E. Fuller, *President*; Howel Williams, *Vice-president*; F. G. Wells, *Secretary*.

Hydrology and Tectonophysics held no elections, the present officers continuing in office as follows:

*Hydrology*—J. E. Church, *President*; L. G. Straub, *Vice-president*; K. H. Beij, *Secretary*.

*Tectonophysics*—E. Cloos, *President*; L. L. Nettleton, *Vice-president*; M. K. Hubbert, *Secretary*.

H. D. Harradon, secretary of the Section on Meteorology, reports that a Committee on Extended Forecasting has recently been established in the Section of Meteorology by Dr. C. W. Thornthwaite, president

of the section. The functions of the committee are (1) to keep abreast of developments in the field of extended forecasting (involving any period in excess of 48 hours); (2) to furnish desired information to agencies or individuals concerning material or publications on extended forecasting and to expedite the preparation of bibliographies on the subject; (3) to furnish opinions on various methods of long-range forecasting to reputable sources desiring such information. These opinions will be based as much as possible on a scientific evaluation of the technique, preferably through objective valuation, and (4) to issue resolutions recommending that certain promising lines of attack on the problem of extended forecasting be encouraged.

The committee consists at present of the following members: Robert C. Elliott, Jerome Namias (chairman), Horace W. Norton, Carl-Gustav Rossby, Harry Wexler and Hurd C. Willett.

## SCIENTIFIC NOTES AND NEWS

THE Faraday Medal of the British Institution of Electrical Engineers, which was awarded last February to Dr. Irving Langmuir, associate director of the Research Laboratories of the General Electric Company, Schenectady, N. Y., was presented to him on June 26 at the St. Louis meeting of the American Institute of Electrical Engineers.

THE Distinguished Service Medal and Award of the American Medical Association for 1944 were conferred at the Chicago meeting on Dr. George Dock, of Pasadena, Calif., formerly professor of medicine at the School of Medicine of Washington University, St. Louis.

DR. ANTON J. CARLSON, emeritus professor of physiology at the University of Chicago School of Medicine, president of the American Association for the Advancement of Science, received the annual Friedenwald Medal at the annual banquet of the American Gastroenterological Association on June 12. The presentation was made by Dr. Andrew C. Ivy, professor and head of the department of physiology and pharmacology of the Medical School of Northwestern University.

THE Royal Asiatic Society of Bengal has awarded the P. N. Bose Memorial Medal for 1943 to Sir Lewis Fermor, formerly director of the Geological Survey of India, "in recognition of his conspicuously important researches on the Archæan Rocks of India."

ABOUT a hundred and fifty university colleagues and friends of Dr. William Albert Riley gathered on May 29 at an informal reception sponsored by the division

of entomology and economic zoology and the department of zoology of the University of Minnesota, as a token of appreciation of his long and fruitful services to the university which culminated with his retirement at the close of the academic year. A number of gifts were presented to Dr. and Mrs. Riley on behalf of the guests participating in the reception.

P. H. BATES, chief of the clay and silicate products division of the National Bureau of Standards, has been chosen president of the American Society for Testing Materials.

SAMUEL B. WILLIAMS, editor of *The Electrical World*, has been elected president of the Illuminating Engineering Society.

NEBRASKA WESLEYAN UNIVERSITY has conferred the degree of doctor of science on Dr. E. I. Fulmer, professor of chemistry at Iowa State College.

THE honorary degree of doctor of science was conferred on June 18 at the ninety-first annual commencement of Antioch College on Dr. Austin M. Patterson, professor emeritus of chemistry.

DR. ALFRED E. COHN, who has reached the age of retirement, has been made a member emeritus of the Rockefeller Institute for Medical Research. Dr. René J. Dubos, George Fabian professor of comparative pathology and professor of tropical medicine at the Harvard Medical School, has been elected a member. Dr. Walther F. Goebel has been promoted from associate member to member, and Dr. Robert F. Watson has been promoted from assistant to associate.



THE retirement on July 1 is announced of Samuel N. Spring, of Syracuse University, dean of the New York State College of Forestry.

DR. GEORGE S. FORBES, professor of chemistry at Harvard University, has been appointed chairman of the department of chemistry.

PROFESSOR RALPH B. WILEY, head of the School of Civil Engineering of Purdue University, has become head of the newly established School of Civil Engineering and Engineering Mechanics, which has been formed by merging the department of applied mechanics and the department of civil engineering.

DR. BENJAMIN HARROW, professor of chemistry of the College of the City of New York, has been elected chairman of the department. He succeeds Dr. William L. Prager.

PROFESSOR RALPH M. HIXON has been named head of the department of chemistry at the Iowa State College. He is also head of the sub-section of plant chemistry of the Agricultural College.

DR. KURT G. STERN, formerly a member of the department of physiological chemistry of Yale University, since 1942 chief research chemist of the Overly Biochemical Research Foundation, New York, has joined the department of chemistry of the Polytechnic Institute of Brooklyn, N. Y. His research at that institution will be conducted under the auspices of the Carrie S. Scheuer Foundation.

AT the University of Oklahoma the following members of the faculty have been promoted to full professorships: Dr. James C. Colbert and Kenneth E. Cook, in chemistry; Dr. Milton Hopkins and Dr. O. J. Eigsti, in plant sciences, and Dr. O. F. Evans, in geology.

THE retirement is announced of Dr. Charles G. Abbot, since 1928 secretary of the Smithsonian Institution, with which he has been connected since 1895. He will continue as research associate of the institution, and plans to devote his time to the study of the physical conditions on the sun.

DR. HUGH H. SMITH, since 1930 a member of the staff of the International Health Division of the Rockefeller Foundation, has been appointed regional director for the United States. He succeeds Dr. John A. Ferrell, who has been made medical director of the John and Mary R. Markle Foundation.

DR. EUGENE M. LANDIS, George Higginson professor of physiology at the Harvard Medical School, has been elected a member of the Council on Pharmacy and Chemistry of the American Medical Association.

FREDERICK R. LACK, vice-president and manager of the Radio Division of the Western Electric Company, was elected a director of the Radio Manufacturers Association at the twentieth annual meeting held in Chicago on June 6 and 7.

AN Ophthalmology Branch has recently been established in the Surgery Division of the Surgeon General's Office with Major M. E. Randolph, Medical Corps, as chief. This branch will concern itself with all matters pertaining to ophthalmology in the Army.

ROBERT E. WATERMAN has been appointed a vice-president and director of the Schering Corporation, pharmaceutical manufacturers of Bloomfield, N. J. He will be associated with the chemical and medical research divisions. Mr. Waterman is a part-time consultant for the alien property custodian as special representative in the production of atabrine.

DR. HORACE S. TELFORD, head of the department of entomology of the North Dakota Agricultural College and Experiment Station at Fargo, has joined the research department of Hess and Clark, Inc., at Ashland, Ohio. He will conduct research in veterinary entomology.

DR. CHARLES F. MEYER, assistant professor of physics in the College of Liberal Arts of Wayne University, has been granted leave of absence by the Board of Education of Detroit. He will work as a research physicist in the laboratory of applied physics of the Johns Hopkins University.

RUSSELL GIBSON, associate professor of economic geology and tutor in the department of geology and geography of Harvard University, has leave of absence and is working with a mining company in South America.

STANLEY F. MORSE, of Winter Park, Fla., agricultural consultant in private practice for the past twenty-five years, is chief of the American Food Mission which has been sent to French North Africa by the U. S. Foreign Economic Administration. The mission will cooperate with and assist the French Committee of National Liberation in its attempts to restore food production to its pre-war volume in Tunisia, Algeria and Morocco. An increased output of foodstuffs is essential in North Africa to help to feed the Allied Armies and the liberated countries of Europe besides saving vital shipping space and relieving the drain on American food supplies. Mr. Morse formerly was director of agricultural extension for the State of Arizona and the U. S. Department of Agriculture. He also has worked in Latin America and in Europe.

PROFESSOR L. H. SNYDER, chairman of the department of zoology and entomology at the Ohio State



University, delivered two lectures at Iowa State College on June 15 and 16. He spoke on "Heredity and Modern Life" and on "The Mutant Gene in Man."

PROFESSOR SIDNEY RUSS, professor of physics at the Medical School, Middlesex Hospital, London, gave on May 20 the twenty-third Silvanus Thompson Memorial Lecture of the British Institute of Radiology. The lecture was entitled "The Man Silvanus Thompson."

DR. E. D. ADRIAN, F.R.S., professor of physiology at the University of Cambridge, gave on June 8 the Bertram Louis Abrahams Lecture at the Royal College of Physicians of London. His subject was "Localization in the Cerebrum and Cerebellum."

THE Zoological Garden of Philadelphia celebrated on July 1 the seventieth anniversary of its founding.

THE *Journal* of the American Medical Association states that this year at its fourth annual meeting in Chicago, the American Diabetes Association on June 11 for the first time awarded the Banting Memorial Medals to all ex-presidents and to all Banting lecturers of the association. The medal was established in honor of Dr. Frederick Banting, who at the time of his death was honorary president of the association. Two medals will be awarded each year, one to the outgoing president and one to the lecturer. Presidents to whom medals have been awarded are Drs. Cecil Striker, Cincinnati; Herman O. Mosenthal, New York, and Joseph T. Beardwood, Philadelphia. Lecturers who have received the award are Drs. Elliott P. Joslin, Boston, first Banting lecturer; Dr. William Muhlberg, Cincinnati, and Colonel Leonard G. Rowntree, M.C. Dr. Joseph H. Barach, of Pittsburgh, was elected president of the association at the recent session. Drs. Russell M. Wilder, Rochester, Minn., and Edward S. Dillon, Philadelphia, were elected vice-presidents.

THE twenty-seventh summer meeting of the Mathematical Association of America will open at Wellesley College, Massachusetts, on August 12, in conjunction with the summer meeting and colloquium of the American Mathematical Society and the meeting of the Institute of Mathematical Statistics. Two sessions of the association will be held on Saturday beginning at 2:30 P.M. and 7:30 P.M. The sessions of the American Mathematical Society will be held on Sunday and Monday. Four colloquium lectures will be given by Professor Einar Hille, of Yale University, his subject being "Selected Topics in the Theory of Semi-Groups." These lectures will be given at 9 A.M. and 2 P.M. on Sunday and Monday. Professor C. C. MacDuffee, of the University of Wisconsin, will give an address at

3:15 P.M. on Sunday, "On the Composition of Algebraic Forms of Higher Degree." A joint session of the association and the Institute of Mathematical Statistics will be held on Saturday evening at 7:30. A reception will be given afterwards by Wellesley College, and on Sunday evening there will be a dinner, followed by a musical entertainment.

THE following is a list of chemicals wanted by the National Registry of Rare Chemicals, Armour Research Foundation, 33rd, Federal and Dearborn Streets, Chicago 16, Ill.: 2-Thio uracil, trimethyl boron, 1,1,1-Tribrom tert. butyl alcohol (Brometone), vinyl trichlor acetate, thallium sulfide, 1,2,5,8-tetrahydroxy anthraquinone, triamino trimethyl amine, sodium salt of nitrohydroxylamine, sodium N,N-diethyl dithiocarbamate, sphingomyelin polyvinyl phthalate, 2-Nitro-4-cyclohexyl acetanilide, methyl nitrite, gray tin (1 g), decaborane, 2,2',2"-tripyrindyl, cadmium xanthate, borobutane and actinium.

A STATE-CONTROLLED hospital program calling for an investment of about \$15,000,000 in five general hospitals, seventy clinics and emergency hospitals and a research laboratory is planned by the State of Arkansas. Additional taxes on natural resources will be necessary for its support, and the question will be submitted to the voters at the next general elections. The act would appropriate \$5,000,000 for each of the fiscal years beginning February 15, 1945, and February 15, 1946. Of the appropriations \$3,500,000 would be for capital expenditures, \$900,000 for general operating expenses, \$500,000 for salaries and \$100,000 for research. Three commissioners would be appointed to seven-year terms by the Governor with the consent of the Senate. They would receive \$5,000 a year. A general auditor and general purchasing agent would receive \$5,000 a year and a secretary-treasurer \$4,200. The commission would fix the duties and the salary of all other employees.

BESTOWED "in recognition of meritorious service rendered to the Army Air Forces Training Command during World War II," a Certificate of Service Award was presented to the Michigan College of Mining and Technology on June 8. The award is signed by Lieutenant-General B. K. Yaunt, Army Air Forces Training Command. Honor guests at the ceremony included Rear Admiral H. S. Kendall, chief of the Air Training Command, U. S. Navy.

*The Times*, London, states that at the first meeting of the British Iron and Steel Research Association Sir James Lithgow was elected president and Dr. Andrew McCance was elected chairman. Immediate steps are being taken to appoint a director of research and a principal administrative officer of the association. In



the meantime, pending completion of the organization of the staff, the Iron and Steel Industrial Research Council will continue to be responsible for the large volume of research which is at present in progress, and the transfer of responsibility for the direction of this will not be made until the new organization is

complete with director and headquarters staff. With the liberal financial provision which has been made by the British Iron and Steel Federation for an expenditure up to £250,000 per annum, a considerable expansion in present research activities is expected immediately the requisite personnel becomes available.

## DISCUSSION

### VARIANTS IN FUNGI: FORMATION, REVERSION AND PREVENTION

AN article by Hansen and Snyder<sup>1</sup> suggests nuclear heterogeneity (heterocaryosis)<sup>2</sup> as the probable cause of losses in ability of *Penicillium notatum* Westling cultures to form penicillin, and suggests remedies. The description of variant strains also applies to variants of *Aspergillus niger* v. Tiegh. obtained through chemical induction by Thom and the writer.<sup>3</sup> Nitrous acid and other compounds were used.<sup>4</sup> Reversion of variants to normal-appearing strains could be brought about by growth on high concentrations of amino acids, particularly lysine. Loss in ability to differentiate was attributed to upsets in the characteristic basal complement of enzymes employed in the utilization of amino acid nitrogen in the normal strain.<sup>5</sup> Inability to differentiate seemed proportional to extent of inability to utilize amino acid nitrogen, particularly hydroxyproline. The culture of *A. niger* employed has proved stable under laboratory conditions for twenty-seven years.

The use of amino acids may prove helpful in recovery of the normal strain of *P. notatum* after variant formation, though in some instances the reversion form is not identical with the initial strain. There is a distinct possibility that a cycle of variant formation and reversion might lead to better penicillin producers for this reason.

Autolyzed cultures of *A. niger* produce variants that seem to be eliminated by culturing at optimum temperature and frequent transfers. The procedure now used to maintain stock cultures in liquid medium includes growth at optimum temperatures until spore formation is well under way and storage in the ice-box at 10° C. until needed.

ROBERT A. STEINBERG

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<sup>1</sup> H. N. Hansen and W. C. Snyder, *SCIENCE*, 99: 264, 1944.

<sup>2</sup> H. N. Hansen and R. E. Smith, *Phytopath.*, 22: 953, 1932.

<sup>3</sup> C. Thom and R. A. Steinberg, *Proc. Nat. Acad. Sci.*, 25: 329, 1939.

<sup>4</sup> R. A. Steinberg and C. Thom, *Proc. Nat. Acad. Sci.*, 26: 363, 1940.

<sup>5</sup> R. A. Steinberg and C. Thom, *Jour. Agr. Res.*, 64: 645, 1942.

### BACTERIOSTATIC AND FUNGISTATIC ACTION OF SOME ORGANIC CHEMICALS<sup>1</sup>

A RECENT abstract in *Chemical Abstracts*<sup>2</sup> reporting the use of sodium selenite in the isolation of paratyphoid bacilli in feces suggested the publication of some observations made in 1940. While attempting to develop a non-sterile technic for studying sugar absorption and assimilation of higher green plants, it was noted that several organic antiseptic chemicals possessed selective bacteriostatic and fungistatic activity.

The results presented in Table I were obtained in

TABLE I  
BACTERIOSTATIC AND FUNGISTATIC ACTION OF SOME ORGANIC CHEMICALS

| Chemical                              | Concn. in p.p.m. | Selective inhibitory action |       |
|---------------------------------------|------------------|-----------------------------|-------|
|                                       |                  | Bacteria                    | Fungi |
| Anisic acid .....                     | 150              | +                           | -     |
| Benzoic acid .....                    | 150              | +                           | -     |
| Chrysoidine Y .....                   | 60               | ±                           | -     |
| Chlorothymol .....                    | 60               | -                           | +     |
| Hexylresorcinol .....                 | 80               | -                           | +     |
| Sodium 2, 4, 5 trichlorophenate ..... | 10               | -                           | ±     |
| 8-hydroxy quinoline sulfate .....     | 10               | -                           | ±     |
| Sodium ortho-phenyl phenate .....     | 60               | -                           | ±     |

Note: (+) Indicates inhibitory action.  
(-) Indicates no inhibitory action.

a diamalt agar media. The cultures were inoculated with a composite mixture of those air-borne micro-organisms which were capable of growing in a liquid media comprised of inorganic nutrients and 0.25 per cent. glucose. The incubation period to determine the selective inhibitory action of the chemicals was six days at 30° C.

The data suggest that some of these chemicals may have possible use in the separation of bacteria and fungi. It will be noted that anisic acid, benzoic acid and possibly chrysoidine Y at the concentrations tested selectively inhibited bacterial growth. Chlorothymol and hexylresorcinol selectively inhibited fungal

<sup>1</sup> Journal Paper No. 161 of the Purdue University Agricultural Experiment Station.

<sup>2</sup> M. A. Gohar. Sodium Selenite as a Bacteriostatic Substance and Its Use in the Isolation of Paratyphoid Bacilli. *J. Trop. Med. Hyg.*, 46: 29-32, 1943. (*Chem. Abst.*, 37: 5995, 1943).



growth. At least at the concentrations used, sodium 2, 4, 5 trichlorophenate, 8-hydroxy quinoline sulfate and sodium ortho-phenyl phenate produced variable fungistatic action. No doubt proper adjustment of concentrations would give more definite results.

These results thus indicate that the use of various bacteriostatic and fungistatic organic chemicals offer a means of separating bacteria and fungi in pathological organism isolation work.

T. M. EASTWOOD

#### ARUBA ISLAND

### EDUCATION IN ARGENTINA

HAVING just returned to the United States after two years spent in Argentina, I can not refrain from passing along a few comments concerning certain changes which are taking place in education there.

Since the revolution of June 3 (1943), the Military Government in the field of education has carried on such policies as attacks upon progressive education and measures against foreigners, repressions in the form of new interventors in the various districts and institutions of higher learning, and affirmative measures emphasizing nationalism, Catholic instruction and totalitarianism in the university field.

In the universities all the deanships have been filled by the appointment of temporary administrators usually of totalitarian sympathy and of clerical stripe. The internal struggle for power within the military clique has resulted in a reshuffling of the ministerial posts and several men have occupied the position of Minister of Justice and Public Instruction. Each change in the position brings about the resignation of each of the interventors assigned to Argentina's six universities. This year, two weeks before the opening of the school year, only one of the six institutions of higher learning had any resemblance to a functional administration.

It may be important to keep scientists informed regarding the situation since under present conditions great caution must be used before further efforts are made by either institutions or individuals to contribute to the betterment of education or scientific research in Argentina. Until there is again freedom of assemblage, freedom of speech and freedom of the press, the opportunities for assisting the educational programs of the country by grants for research, libraries or exchange fellowships are greatly diminished.

J. A. SHELLINGER

KANSAS STATE COLLEGE

## SCIENTIFIC BOOKS

### CHROMOSOMES AND PHYLOGENY

*Contributions to the Genetics, Taxonomy and Ecology of Drosophila pseudoobscura and its Relatives.* By TH. DOBZHANSKY and CARL EPLING. Carnegie Institution of Washington Publication 554. Washington, D. C., 183 pp., 4 plates. Price, \$2.25 (paper), \$2.75 (bound in cloth).

WHEN T. H. Morgan's studies on *Drosophila melanogaster* led to a revolutionary development of the field of genetics, many taxonomists, paleontologists and other naturalists remained sceptical as to the significance of this work. A study of the mutations of a semi-domestic animal in milk bottles, they insisted, might well clear up the mechanics of inheritance and still leave us in the dark on the course of evolution in natural populations. This criticism was well taken, and students of *Drosophila* have turned in recent years with ever-increasing frequency to the outdoor study of wild *Drosophilae*.

Dobzhansky's ten-year work on the *Drosophila pseudoobscura* group finds its culmination in the present publication. A taxonomist by training and an outdoor naturalist by inclination, Dobzhansky was particularly well fitted to engage in research that covers the genetics, taxonomy and ecology of *Drosophila*. In the taxonomic section he shows convinc-

ingly, in joint authorship with Epling, that the so-called races *pseudoobscura* A and B have all the biological characteristics of good species. In spite of the minuteness of the external differences race B is raised to specific rank under the name *D. persimilis*, an action that will be applauded by all biologists to whom the species is more than a receptacle of morphologically similar specimens. The two species *pseudoobscura* and *persimilis*, together with *miranda*, are the only American representatives of the otherwise Palearctic *obscura* group.

The ecological section contains the first thorough account of a wild species of *Drosophila* considerably more detailed and informative than the preliminary descriptions of earlier authors. Particular attention is paid to the factors that affect the population structure, such as food preference, daily cruising radius, population density, daily and seasonal cycles and so forth.

The main body of the book is devoted to a study of the geographical distribution of the various gene arrangements in *pseudoobscura* and *persimilis*. The study of the giant salivary gland chromosomes of the *Drosophila* larvae makes it possible to determine where the chromosomal breaks took place and in what sequence the inversions must have occurred that have



led from the ancestral gene arrangement to the present configuration. The gene arrangements are a morphological character which has two unique advantages over the conventional characters used by the taxonomist. First, the actual genetic basis is studied and not merely a phenotype, and second, the phylogenetic history of each arrangement can be established beyond reasonable doubt.

The mapping of the fifteen known gene arrangements on the third chromosome of *pseudoobscura* and of the seven of *persimilis*, together with a determination of their frequency (in per cent.) throughout the range of the two species allows many interesting conclusions. The theoretically ancestral arrangement *Hypothetical* has not yet been found. Why it should have been replaced by the younger arrangements is an unsolved puzzle. The arrangement *Standard* is the only one that is found jointly in both species, indicating that it was present before *pseudoobscura* and *persimilis* split into two species. Some of the arrangements are apparently very recent since they are still quite localized. The ratio of homozygotes and heterozygotes is so close to the calculated one that random mating and equal viability of the gene arrangements must be expected.

In the final section Epling attempts to correlate the present distribution of the gene arrangements (particularly those with discontinuous ranges) with the geological and climatic history of western North America. He suggests that many of the arrangements are very old and "were in existence during Miocene times or perhaps earlier." This, as it seems to me, highly unlikely conclusion is a striking illustration of the contradictory nature of many of the *D. pseudoobscura* data. On one hand, there is a comparatively high rate of active migration as well as of passive dispersal; on the other hand, there is an almost unbelievable localization of populations as indicated by genetic differences between populations less than a mile apart. On one hand, there are clinal changes of frequency in the *Klamath*, *Standard*, *Arrowhead* and *Pikes Peak* arrangements, which seem to parallel closely climatic changes. On the other hand, some arrangements are equally at home in such contrasting climatic provinces as the interior of British Columbia, the mountains along Death Valley and the plains of Texas. I can not escape the feeling that a joker is hidden somewhere in this deck of cards. Perhaps this discrepancy can be explained by assuming an even greater selective significance of small genetic differences than was previously realized. This would counterbalance the swamping that undoubtedly must take place continuously. A study of the endemic *Drosophilidae* of the oceanic Hawaiian Islands might shed some light on the passive dispersal facilities of this family.

Finally, the absence of the *Santa Cruz* arrangement from the most arid section of the southwestern deserts, as well as the seasonal fluctuation of the gene arrangements in at least two localities in California indicate that some inversions may have different selective values in different environments. To be sure, as Dobzhansky himself points out (*Genetics*, 28: 179, 1943), it is not the inversions themselves that produce these effects, but rather the genes that are variously associated with them at each locality. The possible role of a position effect of such breaks should not be overlooked. Perhaps the reduction of crossing over permits the development of stabilized gene complexes with very specific properties.

This work has all the earmarks of one of the classics of the field of genetics. It is rich in fact and rich in thought-provoking discussions. It is pioneering in its employment of new methods and exemplary in its coordination of the three fields of genetics, taxonomy and systematics.

E. MAYR

THE AMERICAN MUSEUM OF  
NATURAL HISTORY

### SYNTHETIC RUBBER

*Synthetic Resins and Rubbers.* By PAUL O. POWERS.  
New York: John Wiley and Sons, Inc. 296 pages.  
\$3.00.

EVER since the Japanese invaded Malaya, every one has been aware that the source of supply of natural rubber was cut off from us. It is also a well-known fact that colossal strides have been made by technologists to fabricate various types of synthetic rubber out of raw materials available in this country. A book, therefore, which discusses the chemistry of synthetic rubbers is timely.

As the title indicates, the subject of this book is both resins and rubbers. Rubber, synthetic or natural, is but one of a large class of organic compounds. Other products which likewise fall into this category are plastics, synthetic resins, adhesives, coating compositions, paints, varnishes and lacquers and synthetic fibers. One fundamental property which all these materials possess is that they are very large and complex organic molecules. It follows that, since these materials are fundamentally related, their uses are also often interchangeable. For example, natural rubber has been used as an adhesive, as a fiber, as a coating composition and as a molding compound. Conversely, certain resinous materials may be used as rubbery materials and as fibers.

Under appropriate conditions, a great many simple organic compounds can be transformed into derivatives whose molecular weight varies from 500 to 500,000 and perhaps even much higher. Compared to



simple chemical compounds, these products are giants from 30 to 30,000 times as heavy as a molecule of water.

It is the purpose of this book to describe methods by which this chemical transformation or polymerization may be achieved. The description is limited to those products which have achieved commercial importance. Theories of polymer formation (52 pages), condensation polymers (62 pages), vinyl polymers (59 pages), synthetic rubbers (57 pages), resins derived from natural products, particularly rubber and cellulose (37 pages), and application of synthetic resins (24 pages), are adequately treated. The author uses the pragmatic approach and makes a distinction

between polymers formed by condensation and those secured by polymerization. This method is useful and adds to the ready presentation of those products where both types of reaction mechanisms are used to bring about an increase in the molecular weight. To each chapter is appended a series of review questions and a good selection of special and, where possible, general references.

The book is recommended to any one who desires a concise summary of the chemistry of synthetic resins and rubbers.

E. L. KROPA

AMERICAN CYANAMID COMPANY,  
STAMFORD, CONN.

## SPECIAL ARTICLES

### AGGREGATION IN SOLUTION OF A SYNTHETIC HAPTEN

A SYNTHETIC hapten which precipitated specifically with antibody was first produced by Landsteiner and van der Scheer.<sup>1</sup> Later Marrack<sup>2</sup> pointed out that if a theory of serological reactions which we may refer to as the "alternation" (or "framework") hypothesis<sup>3</sup> is correct, any compound containing as many as two specific groups capable of combining with antibody should be able to form a precipitate; and this prediction was later tested by Hooker and Boyd,<sup>4</sup> by Pauling and collaborators<sup>5</sup> and by Boyd.<sup>6</sup> In some of these experiments precipitation of hapten by antibody was observed, and Pauling has stated that he considers that these "phenomena provide strong support for the framework theory of serological precipitates. . . ."

It should be recalled, however, that Landsteiner<sup>7</sup> considered that the precipitability of the haptens studied by him was due to their being aggregated in solution, and Hooker and Boyd<sup>4</sup> pointed out that if the haptens studied by Pauling were aggregated under the conditions of the tests this would considerably weaken the support given the theory by this evidence. They further reported observing differences in diffusibility into gelatin of precipitable and non-precipitable haptens, which did in fact suggest that the precipitable ones were aggregated.

We have attempted to study the question of the

degree of aggregation in solution of such precipitable haptens, and wish to report here observations made on an arsanilic-phloroglucinol derivative, designated as "VII" in Pauling's earlier paper and in the paper by Boyd<sup>6</sup> and as "XI" in Pauling's later papers. To estimate the degree of aggregation we made measurements of the diffusion coefficient, using the sintered glass disk technic as employed by Northrop and Anson,<sup>8</sup> McBain and others,<sup>9</sup> Lehner and Smith,<sup>10</sup> and Mehl and Schmidt.<sup>11</sup> The disks used were calibrated with both KCl and sucrose.

For hapten "VII" ("XI") we have found a diffusion coefficient at 25° of about 0.109 cm<sup>2</sup>/day, which would indicate, if the particles are spherical, a particle size in the neighborhood of 12,500. Since the formula weight is 1,122, this would indicate that the hapten is aggregated in solution to the extent of about 10-12 molecules per particle. Details will be published elsewhere.

If other precipitable haptens are aggregated in solution, as we suspect at least some of them are, it is evident that the fact of their precipitability is no stronger evidence for the "alternation" theory than is the precipitation of any antigen, since it seems likely that each particle of the aggregate will have quite a number of accessible specific reacting groups, just as ordinary antigens do. It is evident therefore that we shall in that case have to reexamine most of the conclusions which have been drawn by Pauling and others from experiments with such substances. In particular Pauling's calculations of antibody valence become doubtful.

<sup>1</sup> "The Specificity of Serological Reactions," Springfield, 1936.

<sup>2</sup> *Jour. Gen. Physiol.*, 12: 543, 1928-29.

<sup>3</sup> *Jour. Am. Chem. Soc.*, 53: 59, 1931.

<sup>4</sup> *Jour. Am. Chem. Soc.*, 57: 497, 1935.

<sup>5</sup> *Univ. of Calif. Pub. in Physiol.*, 8: 165, 1937.

<sup>6</sup> *Proc. Soc. Exp. Biol. and Med.*, 29: 747, 1932; *Jour. Exp. Med.*, 56: 399, 1932.

<sup>7</sup> "The Chemistry of Antigens and Antibodies," H.M. Stationery Office, London, 1938.

<sup>8</sup> S. B. Hooker and Wm. C. Boyd, *Jour. Immunol.*, 42: 419, 1941.

<sup>9</sup> *Arch. Path.*, 28: 754, 1939; *Jour. Immunol.*, 42: 419, 1941.

<sup>10</sup> *Proc. Nat. Acad. Sci.*, 27: 125, 1941; *Jour. Am. Chem. Soc.*, 64: 2994, 1942.

<sup>11</sup> *Jour. Exp. Med.*, 75: 407, 1942.



We are indebted to the Rockefeller Foundation for financial support of this work.

WILLIAM C. BOYD  
JANE BEHNKE

SCHOOL OF MEDICINE,  
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**RAW HEN EGG WHITE AND THE ROLE OF  
IRON IN GROWTH INHIBITION OF SHI-  
GELLA DYSENTERIAE, STAPHYLO-  
COCCUS AUREUS, ESCHERICHIA  
COLI AND SACCHAROMYCES  
CEREVISIAE<sup>1</sup>**

RAW hen egg white can cause an inhibition of growth of *Shigella dysenteriae* and other microorganisms which is independent of the avidin-biotin phenomenon. Of ten vitamin factors and thirty-one elements tested, iron alone overcame this egg white inhibition.

In the course of work on the stabilization of dysentery bacteriophage during lyophilization, secondary growth of a strain of *S. dysenteriae* failed to appear in the first tube of a d'Herelle titration of a phage sample lyophilized with raw egg white. Titrations run in the absence of phage with varying concentrations of egg white showed that the inhibition of growth depended upon the amount of egg white added to the medium and was not related to phage activity. 0.02 ml of egg white per ml of nutrient broth (0.3 per cent. Lemco meat extract, 1.0 per cent. Bacto peptone, 0.5 per cent. sodium chloride, adjusted to pH 7.2) inhibited the development of  $2-20 \times 10^5$  bacteria for 24 hours at 37° C. Serial dilution of transfers made from the inhibited cultures to fresh egg white-free broth showed that failure to grow was not due to destruction or lysis of the bacterial cells.

Additions of avidin concentrate to the nutrient broth in an amount equal to twice the estimated avidin content of an inhibiting concentration of raw egg white failed to prevent normal growth of *S. dysenteriae*. Conversely, additions of biotin to the egg white-treated broth in an amount estimated to be twice that required to neutralize the avidin content of the contained egg white failed to permit normal growth of the bacteria.

The effect of pH on the inhibition phenomenon by egg white was such that at pH of 5.8 and below, bacterial growth occurred equal to controls without egg white; at pH's between 5.8 and 6.4, partial inhibition was exerted so that as the pH approached 6.4, initiation of growth was increasingly delayed; at pH 6.4 and above, inhibition of growth was complete for at least 48 hours at 37° C.

When raw egg white was dialyzed against distilled water, the dialyzed material retained fully its ability to inhibit the growth of the bacteria while the dialyzate

<sup>1</sup> A preliminary report.

was without effect. Further, heating samples of egg white adjusted to pH 7.3 with phosphate buffer in nutrient broth for one hour at 40° C., 50° C., 60° C. and 70° C. showed that the inhibiting capacity of the raw egg white is stable at temperatures up to 60° C. but destroyed at 70° C. under the conditions employed.

Corn steep liquor, meat extract and yeast extract, when added in relatively large amounts to nutrient broth in the presence of egg white, permitted growth of *S. dysenteriae* to occur equal to controls without egg white. The following known growth factors were tried singly and in combination: thiamin hydrochloride, riboflavin, nicotinamide, inositol, calcium pantothenate, pyridoxine, biotin, para aminobenzoic acid, choline chloride and tryptophane. All were ineffective in overcoming the egg white inhibition.

When yeast extract was ashed, however, the ash after solution in hydrochloric acid was active. Of 31 elements tested, iron alone overcame the egg white inhibition of growth. Soluble ferrous and ferric salts were effective when used in an amount of approximately 20 gammas of iron for every ml of raw egg white, the ferrous iron being consistently somewhat more active than the ferric form. The amount of "free" iron (dipyridyl method) in the 4.5 ml of nutrient broth used routinely was 0.8-1.0 gammas. Since one ml of egg white requires 20 gammas of added iron, 0.04 to 0.05 ml might be expected to make the "free" iron of the broth unavailable to the bacteria for growth. In general, the results obtained justify this expectation.

Ferrous and ferric ammonium sulfate were added to egg white at various pH's and dialyzed overnight at room temperature against buffered saline. Qualitatively, the data obtained showed that at pH 7.0 and above egg white made both forms of iron undialyzable; at pH 6.0 and to a greater extent at pH 5.0, some ferrous iron could be dialyzed, while ferric iron was undialyzable at both pH's. All results were compared to controls of iron alone in buffered saline at the same pH's. The effect of pH on the dialyzability of iron from egg white-iron salt mixtures finds some parallel in the relation of pH to the inhibition of growth of *S. dysenteriae* in egg white-treated nutrient broth.

When ferric or ferrous iron in concentrations employed in this study were added to raw egg white, a tan to brownish coloration appeared. The depth of color varied directly with the amount of iron added. Possible correlation of color production with the biological phenomenon reported here is being investigated.

Preliminary study of the inhibitive effect of raw egg white on the growth of a strain of *Staphylococcus aureus*, *Escherichia coli* and *Saccharomyces cerevisiae*



(Fleischmann No. 139) was made. *S. aureus*, non-extracting with respect to biotin, showed an egg white sensitivity similar to *S. dysenteriae*. The less sensitive *E. coli* was only slightly retarded in its rate of growth. *S. cerevisiae*, in the presence of excess biotin in a 1 per cent. sucrose nutrient broth at pH 7.0, was completely inhibited by a 1/20 dilution of egg white. At pH 6.0 this inhibition was strongly marked but not complete. Iron addition, either ferrous or ferric, overcame the egg white inhibition shown by all the organisms tested.

The foregoing results suggest that the ability of raw egg white to combine with iron and make it unavailable to microorganisms for growth may have significance for diagnostic and therapeutic purposes as well as for biological phenomena in which egg white and/or iron are known to, or may, play an important role. Thus, in animal nutrition, the egg white injury syndromes may find explanation in deficiency not only of biotin but also of iron induced either directly in the host or indirectly through modification of the intestinal flora. Egg white might be used to advantage as a tool in the study of various anemias or of perosis and other multiple deficiency diseases with reference to possible involvement of iron.

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#### AN OXIDATIVE METABOLITE OF PYRIDOXINE IN HUMAN URINE

In 1941 Singal and Sydenstricker described in a brief note in this journal<sup>1</sup> the appearance of a fluorescent compound in human urine after the ingestion of pyridoxine ( $B_6$ ). No further studies were reported concerning its nature. We confirmed this observation and also found that upon heating the urine with acid this substance is converted to a new compound possessing a fluorescence of maximum intensity at above pH 8.6 as compared with a maximum at pH 3-4 for the original substance. Moreover, the fluorescence intensity of the new substance is 25 times greater.

This new fluorescent substance was isolated in crystalline form from urine heated with acid. Since this product was easily reduced (with hydrosulfite) to a non-fluorescent form and reoxidized (with  $H_2O_2$ ) to the original form it was surmised to be an oxidation product. Employing a slow direct oxidation of  $B_6 HCl$  with permanganate in neutral solution a product was obtained which appears to be identical with the urinary substance, as shown by the data in Table 1.

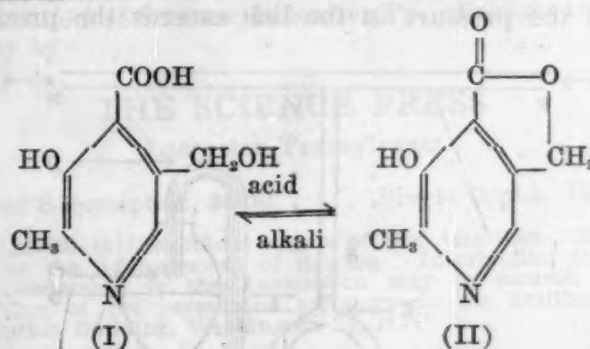
<sup>1</sup> S. A. Singal and V. P. Sydenstricker, *SCIENCE*, 94: 545, 1941.

TABLE 1

| Compound  | M.P. (II) | Mixed M.P. | M.P. of methyl ether of (II) | Mixed M.P. | Fluorescence* (II) | (I) |
|-----------|-----------|------------|------------------------------|------------|--------------------|-----|
| Synthetic | 263-5°    | 263-5°     | 111-2°                       | 111-2°     | 1300               | 52  |
| Urinary   | 263-5°    |            | 111-2°                       |            | 1300               | 52  |

\* The fluorescence is expressed in galvanometer divisions per microgram per cc in the Coleman Electric Photofluorometer employing filters B1 and PC1.

The structure of this compound was shown to be the lactone of 2-methyl-3-hydroxy-4-carboxy-5-hydroxymethyl pyridine (II),<sup>2</sup> which is converted by heating with alkali to the corresponding acid form (I). This is the form (I) in which the oxidative product is excreted in human urine after the ingestion of  $B_6$ . The intensity of the fluorescence of the two compounds varies with the pH of the solution according to well-defined curves different and characteristic for each of them.



After the ingestion of 50 mg of  $B_6 HCl$  normal human adults excrete 3-8 mg of compound (I) in 4 hours, and 200-300 mg in 24 hours after the ingestion of 1 gram. It is not excreted by dogs and is excreted to a small extent by rats after the administration of the vitamin. Our observations indicate that it is not identical with the metabolites of  $B_6$  studied in these 3 species by Scudi and collaborators.<sup>3</sup>

The details of the isolation and identification of the compounds as well as of a method for their quantitative determination will be published elsewhere.

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<sup>2</sup> The isomer of this compound, the lactone of 2-methyl-3-hydroxy-4-hydroxymethyl-5-carboxy pyridine was synthesized and described by S. A. Harris, E. T. Stiller and K. Folkers, *Jour. Amer. Chem. Soc.*, 61: 1242, 1939, in the course of the elucidation of the structure of vitamin  $B_6$ . We are greatly indebted to Dr. K. Folkers of Merck and Company for a sample of this isomer which aided us materially in establishing the structure of the metabolite described in this paper.

<sup>3</sup> J. V. Scudi, R. P. Buhs and D. B. Hood, *Jour. Biol. Chem.*, 142: 323, 1942.

<sup>4</sup> Nutrition Foundation Fellow. The authors are also indebted for grants in aid of this study to the John and Mary Markle Foundation and the Duke University Research Council; and to Merck and Company, Inc., for a generous supply of pyridoxine.



## SCIENTIFIC APPARATUS AND LABORATORY METHODS

## A MANOMETRIC VALVE OR RESPIRATOR

THIS valve permits of a fully automatic increase and decrease in pressure, over a variable fixed range, in reaction or culture vessels or rooms; and it obviates the discharge of, and consequent replacement of, waste liquid from the valve. Mercury is added to the separatory funnel so as to establish a liquid level B, higher than the point of intersection E in the inverted glass Y (FGH). At this time the mercury is continuous from level B, down through the U tube LKF, and in the legs of the Y (FE and EG). The introduction of gas under pressure at N then forces the mercury in the Y down through the two legs (FE and EG), into the capillary GM and into one arm (FK) of the U tube FKL. As the pressure in the line RN approaches a maximum, the mercury initially contained in EG approaches the upper limit A of the capillary tube. When the pressure in the line exceeds the pressure

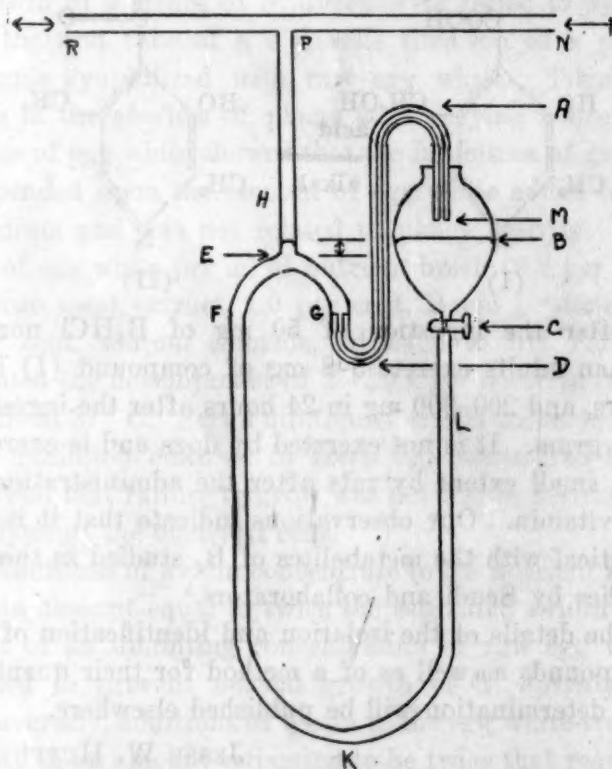


FIG. 1. A separatory funnel, a piece of capillary tubing, and an inverted glass Y are connected as illustrated.

represented by a column of mercury of vertical distance AD, all the mercury in the capillary spills over into the separatory funnel. The positive pressure in the line RN then drops as gas escapes through the now open capillary. The pressure of the mercury in the funnel then forces up the depressed mercury level in FK until the mercury once again spills over through FE into EG. The valve is thereby closed and the above cycle repeats.

The pressure range over which the valve operates is primarily a function of the vertical distance AD.

Other variables, of which the rate of pressure increase and pressure decrease are a function, include: the rate of flow of gas into the line RN; the capacity of the chambers into which and out of which the gas flows through RP; the diameter of the capillary in the capillary tube; the capacity and angle of inclination of leg EG of the Y; the vertical distance EB which determines the hydrostatic pressure responsible for the return of the mercury from the funnel to the Y; and the setting of the stopcock C. These variables may be manipulated to suit one's purpose.

A valve of this type has been used to breathe cultures of microorganisms grown upon and within porous masses, that is, in the study of metabolizing masses which otherwise offer resistance to uniform aeration and temperature control. The rate of replacement of the gases in the reaction or culture vessels may be controlled by interposing a baffle between the line PR and the culture vessels, or by recirculating the gases expelled from the capillary at M, instead of permitting those gases to escape into the atmosphere. One of the obviously related uses for this respirator may be found in the study of respiratory quotients at gas-liquid-solid interfaces, in surface metabolism, as supplementary to the techniques in common use at the present time.

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